

Atty Dkt. No.: UCAI-199  
USSN: 09/990,102

### REMARKS

In view of the above amendments and the following remarks, the Examiner is respectfully requested to withdraw the rejections and allow Claims 1-20.

Claims 1, 6, 15 and 16 have been amended to specify the evaluation of an observed data set to identify a nucleic acid specific signal. Support for these amendments may be found throughout the specification, e.g., in the experimental section such as at page 40, line 25 to page 41, line 25.

As no new matter has been added by the above amendments, the Applicants respectfully request the entry thereof.

### Rejection under 35 U.S.C. §103(a)

Claims 1-16 have been rejected under 35 U.S.C. §103(a) as obvious over Chan (WO 98/35012). The M.P.E.P. provides clear guidance on the requirements of a *prima facie* case of obviousness:

To establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations. M.P.E.P. § 2142.

Accordingly, in order to render the claims obvious, Chan must teach or suggest all of the claim limitations. As noted above, independent Claims 1, 6, 15 and 16, and the claims that depend therefrom, have been amended to specify that that the obtained set of observed data values is evaluated to identify a duplex nucleic acid specific signal.

However, Chan does not teach or suggest the characterization of a duplex nucleic acid based on the identification of a duplex nucleic acid specific signal (Claim 1), or the presence of a duplex nucleic acid based on the identification of a duplex nucleic acid specific signal (Claim 6), or a nanopore device or kit that includes an algorithm for characterizing a duplex nucleic acid based on evaluating observed current modulations through a nanopore to identify a duplex nucleic acid specific signal (Claims 15 and 16).

Specifically, Chan does not teach or suggest the passage of a duplex nucleic acid through a nanopore and the identification of a signal that is indicative of a duplex nucleic acid, i.e., the identification of a duplex nucleic acid specific nucleic acid signal. More specifically, the subject claims

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specify that a signal is identified as a duplex nucleic acid signal. Stated otherwise, the identified signal is indicative of a duplex nucleic acid molecule contacted with the nanopore such that the signal identified as a duplex nucleic acid specific signal is distinct from a signal that would be identified as a single stranded nucleic acid specific signal, i.e., a signal that would be identified if a single stranded nucleic acid molecule were to be contacted with the nanopore. However, nowhere does Chan describe the identification of a signal as a duplex nucleic acid specific signal (as opposed to a single stranded nucleic acid specific signal) and in fact Chan does not describe the differentiation of a duplex nucleic acid signal from a single stranded nucleic acid signal at all, let alone by identifying a signal based on observed data values obtained from a nanopore. Chan is mainly directed towards labeling polymers with fluorescent labels or other analogous labels and detecting these labels, e.g., as the labeled polymer is passed through a nanopore. For example, Chan described that in a preferred embodiment that the signal that is generated by the interaction between the unit and the agent results from fluorescence resonance energy transfer (FRET) between fluorophores (see, e.g., page 35, first para. to page 40, line 21; and page 42 line 13 to page 55, line 18).

Furthermore, the Examiner contends that Chan teaches the detection of specific feature information for the polymers analyzed and refers to Chan's disclosure that "the polymer specific feature is information about a structural feature of a polymer" to support the assertion that this renders the claims obvious in regards to characterizing a duplex nucleic acid with a signature current blockade profile. However, the teachings of Chan referred to by the Examiner are merely general teachings regarding obtaining information about a polymer based on polymer specific features and as such do not describe the identification of duplex nucleic acid specific signal based on an observed data set obtained by monitoring current changes through a nanopore, as specified in Claims 1, 6, 15 and 16, as amended.

Accordingly, Chan does not teach or suggest all the claim limitations of Claims 1, 6, 15 and 16, and the claims that depend therefrom, for at least the reason that Chan does not teach or suggest the characterization or detection of a duplex nucleic acid by the identification of a duplex nucleic acid specific signal, since Chan provides no teachings or suggestions that duplex nucleic acids yield signals that are distinguishable from single stranded nucleic acids.

In regards to Claim 13, the Applicants respectfully submit that Chan does not render this claim obvious as Chan fails to teach or suggest all of the claim limitations. Specifically, Claim 13 specifies a method of determining the sequence of a duplex DNA molecule that includes providing a duplex DNA molecule that is protected at one end and blunt ended at the other end and producing a single nucleotide overhang at the blunt end. However, Chan does not teach or suggest a provision of a duplex DNA

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molecule that is protected at one end and blunt ended at the other end and producing a single nucleotide overhang at the blunt end. Consequently, Chan does not teach or suggest contacting the duplex DNA having a single nucleotide overhang with a nanopore and applying an alternating electric field to the nanopore and monitoring current changes through the nanopore to obtain a set of observed values, also as claimed in Claim 13.

Furthermore, Claim 13 specifies the removal of the single nucleotide overhang from the duplex DNA molecule and repeating the steps of producing a single nucleotide overhang at the blunt end, contacting the duplex DNA having a single nucleotide overhang with a nanopore, applying an alternating electric field to the nanopore, monitoring current changes through the nanopore to obtain a set of observed values, thus to obtain a collection of observed values for each different duplex nucleic acid produced from the original duplex nucleic acid, and determining the sequence of the duplex DNA molecule from the collection of observed data values. As Chan does not even teach or suggest a provision of a duplex DNA molecule that is protected at one end and blunt ended at the other end and producing a single nucleotide overhang at the blunt end and contacting such a duplex DNA molecule with a nanopore and applying an alternating electric field to the nanopore and monitoring current changes through the nanopore to obtain a set of observed values, Chan does not teach or suggest the removal of the single nucleotide overhang from the duplex DNA molecule and repeating the above-described steps to obtain a collection of observed values for each different duplex nucleic acid produced from the original duplex nucleic acid and determining the sequence of the duplex DNA molecule from the collection of observed data values. Accordingly, Chan does not teach or suggest all the claim limitations of Claim 13.

Accordingly, for at least the reasons described above, Chan does not teach or suggest all of the claim limitations of Claims 1-16. As such, the Applicants respectfully request that this rejection be withdrawn.

#### Allowance

The Applicants thank the Examiner for the indication of allowance of Claims 17-20.

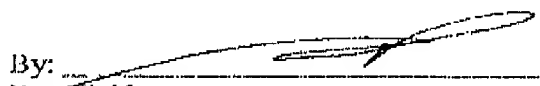
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### CONCLUSION

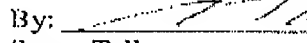
In view of the above amendments and remarks, this application is considered to be in good and proper form for allowance and the Examiner is respectfully requested to pass this application to issuance. The Commissioner is hereby authorized to charge any underpayment of fees associated with this communication, including any necessary fees for extensions of time, or credit any overpayment to Deposit Account No. 50-0815, Order No. UCAL199.

Respectfully submitted,  
BOZICEVIC, FIELD & FRANCIS LLP

Date: 8/6/03

By:   
Bret Field  
Registration No. 37,620

Date: 8/6/03

By:   
Susan Tall  
Registration No. 52,272

BOZICEVIC, FIELD & FRANCIS LLP  
200 Middlefield Road, Suite 200  
Menlo Park, CA 94025  
Telephone: (650) 327-3400  
Facsimile: (650) 327-3231